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16. ABSTRACT

(Project Officer: Daniel Greathouse)

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Arsenic Levels in Human Blood, Urine, and Hair in Response to Exposure via Drinking Water

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Five communities with water supplies having arsenic concentrations of 6, 51, 98, 123, and 393 μg/liter were selected for study. Samples of blood, hair, urine, and tap water were obtained from participants in each community and analyzed for arsenic content. Results showed an increase in arsenic concentration for urine and hair samples as the water arsenic concentrations increased. Arsenic levels in blood did not show this trend until chronic toxicity was expected. We conclude that arsenic levels in water at concentrations of 100 μg/liter or less seem not to produce an undue body burden.

INTRODUCTION

Arsenic exposure has been associated with various disease states. In humans it has been linked to cancer (Bettley and O'Shea, 1975; Blot and Fraumeni, 1975; Jhaveri, 1958; Ott *et al.*, 1974; Tay and Seoh, 1975), cardiovascular disease (Barry and Herndon, 1962; Rosenberg, 1974; Grobe, 1976), and neurological effects (Ohta, 1970; Conrad *et al.*, 1976). The same disorders have been linked by other investigators to arsenic exposure via drinking water when concentrations of the element exceed the U.S. drinking water standard of 50 μg/liter (Borgoño and Greiber, 1971; Morton *et al.*, 1976; Tseng *et al.*, 1977).

In many of the studies cited, tissues such as hair or blood were used to determine if an increase in arsenic levels in the body would aid in explaining the health effects observed. However, no consistent choice of body tissue or fluid was made among the investigators.

There have been no reports of an increase in arsenic levels in biological specimens for large population groups, each exposed to one arsenic concentration from a single source and at increasing levels of exposure for each community. Such information would afford an assessment of the effect of increasing arsenic consumption on body stores. The study of Goldsmith and co-workers (1972), evaluating the effects of a population using water from individual wells with elevated concentrations of the element, is the report that comes closest to such an assessment. However, in his evaluation, only individual observations for a single tissue, hair, were used. The results obtained seemed to indicate that arsenic levels in hair begin to rise above 0.1 μg/g when the well water concentration increases above 50 μg/liter.

We were afforded the opportunity to measure concentrations of arsenic in several tissues for different populations, each of which was exposed to a different concentration of arsenic in its drinking water. Such an attempt allowed us to reassess the effect of increasing arsenic concentrations in drinking water on the resultant body burden when several observations were possible at a given expo-

sure level. In addition, we were able to judge which tissue (hair, blood, and/or urine) best reflects body burden as a result of exposure.

MATERIALS AND METHODS

Five study communities, each receiving different levels of arsenic in their water supply, were chosen. The communities were Fairfax and Edison in Bakersfield, California and Virginia Foothills, Hidden Valley, and Fallon from Nevada. Their respective arsenic concentrations were 6, 393, 51, 123, and 98 μg/liter. These levels served to bracket the U.S. drinking water standard of 50 μg/liter.

Households, randomly selected when the exposed community was too large to be examined completely, were used to obtain participants. When possible, samples of scalp hair, 24-hr urine, and blood were obtained from each participant and a sample of tap water from each household. A questionnaire was administered to determine the length of residence, dietary habits, and occupational history. No participant was included in the study unless he had used his present water supply for at least 1 year.

Sample preparation of hair consisted of thorough washing of samples with nonionic detergent, ethyl alcohol, and distilled–deionized water rinse. The entire hair sample was used for analysis. It was assumed that this study population was in a steady state with respect to intake and excretion of arsenic since individuals were included only if their length of residence in the community was more than a year.

Hair samples so prepared and whole blood, urine, and water samples were wet ashed with nitric and perchloric acid. Arsenic in the digested samples was analyzed by the procedure described by Kang and Valentine (1977). The method involved reducing the arsenic with sodium borohydride followed by analysis of the generated arsine on an atomic absorption spectrophotometer, Perkin–Elmer Model 303.

The U.S. EPA reference trace-metal standard was analyzed with each set of biological samples. In every case, accuracy was within ±5% of EPA's value.

Statistical analysis consisted of the χ^2 and Student's t test.

TABLE 1
DEMOGRAPHIC PROFILE OF COMMUNITIES

	Fairfax	Virginia Foothills	Fallon	Hidden Valley	Edison
Age*	35 ± 16[a] (14–65)[b]	44 ± 14 (14–65)	41 ± 18 (10–76)	40 ± 16 (9–62)	26 ± 15 (6–59)
Sex	F 62% M 38%	F 50% M 50%	F 59% M 41%	F 64% M 36%	F 60% M 40%
Years lived in community*	9.6 ± 8 (1–28)	4.3 ± 2.8 (2–13)	8.7 ± 7.3 (2–37)	8.1 ± 3.8 (3–15)	6.4 ± 4.2 (1–13)
Percentage of smokers	30.7	36	41.2	22.7	43

[a] Mean ± SD.
[b] Numbers in the parentheses indicate ranges.
*Significantly different ($P < 0.05$) among the communities.

TABLE 2 ARSENIC CONCENTRATIONS IN HUMAN BLOOD, URINE, HAIR, AND WATER SAMPLES

Sample	Community	Present study			Reported in literature			
		No. of samples	Mean ± SD	Range	No. of samples	Mean ± SD	Range	References
Blood (μg 100 ml)	Edison	33	1.33 ± 1.18	0.18–5.5	11	0.69 ± 0.76	0.0–2.8	Baumler *et al.* (1968)
	Fallon	38	0.29 ± 0.18	0.03–0.85				
	Hidden Valley	21	0.42 ± 0.17	0.08–0.73	—	0.25 ± 0.05[a]	—	Heydorn (1970)
	Virginia Foothills	28	0.51 ± 0.65	0.01–3.50	5	4.6 ± 2.19	3–7	Wagner and Weswig (1974)
	Fairfax	24	0.49 ± 0.12	0.25–0.74				
Hair (μg g)	Edison	35	1.16 ± 0.80	0.36–4.31				
	Fallon	45	0.57 ± 0.45	0.08–2.42	58	0.33 ± 0.23	<1.0	Boylen and Hardy (1967)
	Hidden Valley	21	0.50 ± 0.37	0.01–1.39				
	Virginia Foothills	25	0.48 ± 0.44	0.07–0.44		0.51[b]	0.25–.88	Camp and Gant (1949)
	Fairfax	10	0.15 ± 0.11	0.04–0.39	1200	0.66[b]	—	Smith (1962)
Urine (μg day)	Edison	35	229.26 ± 200.92	10.12–924.0				
	Fallon	46	80.26 ± 45.38	10.85–227.12	5	73 ± 72.5	24–201	Wagner and Weswig (1974)
	Hidden Valley	22	70.47 ± 38.18	5.7–153.14	50	84 (μg/liter)[b]	12–325	Smith (1962)
	Virginia Foothills	28	63.07 ± 56.71	10.98–280.8	—	40 (μg/liter)[b]	—	Heyman *et al.* (1956)
	Fairfax	32	10.9 ± 7.9	3.05–38.45	6	23 ± 31 (μg/liter)	2–83	Baumler *et al.* (1968)
Water (μg liter)	Edison	16	393.06 ± 31.24	328–462				
	Fallon	23	98.24 ± 2.15	95–105				
	Hidden Valley	10	122.80 ± 16.48	107–163				
	Virginia Foothills	17	51.24 ± 12.74	33–76				
	Fairfax	17	<6.0					

[a] Standard error of mean. [b] No standard deviation given.

RESULTS

The demographic profiles of the five communities are summarized in Table 1. By the χ^2 test, the distribution of sex, race, and smoking were not significantly different; however, age and years lived in the community were statistically different ($P < 0.05$). No apparent difference in arsenic body burden due to these variables was expected or found. No occupational exposure or undue intake via food was observed. It was concluded, therefore, that the study populations were comparable to each other for the purpose of this study.

The range and average concentrations of arsenic in tap water, whole blood, hair, and urine for each community are given in Table 2, along with the range and average concentrations for the same biological specimens for unexposed populations of normal individuals as reported by others in previous studies.

The mean concentrations for blood arsenic were somewhat larger than values previously reported by Heydorn (1970) and Baumler and co-workers (1968). When the present arsenic values were compared to data reported by Wagner and Weswig (1974), our blood arsenic values were lower for all communities except Edison. From our data and that previously reported, it seems arsenic concentrations for human blood vary widely depending on different analytical methods.

For each community except Edison, the mean concentrations for arsenic in hair and urine are similar to values previously reported. Edison's mean value was higher, reflecting the higher content of the element in the Edison water supply. Hair and urine arsenic concentrations for the Fairfax community, which had essentially no arsenic exposure, were below values previously reported for unexposed populations and below values obtained for the arsenic communities presently surveyed. It should be noted that although different analytical methods were employed for hair analyses and for urine analyses, the values obtained by different researchers for body samples agree closely.

Figures 1 through 3 show, for the five study populations, mean arsenic level in the tap water. The mean arsenic levels of hair and urine showed similar patterns of increasing concentrations with increasing exposure level. The blood levels did not

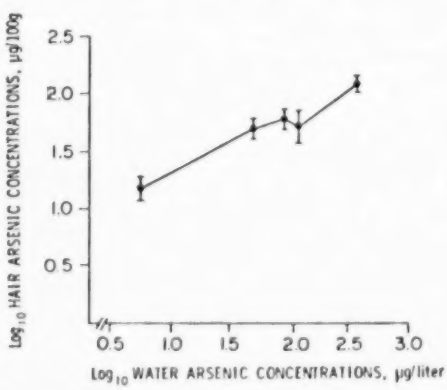

FIG. 1. Mean hair arsenic concentration plotted as a function of mean arsenic concentration in tap water for compared communities. The bars represent standard error of mean.

al. (1968)

	Edison	16	393.06 ± 31.24	328–462
	Fallon	23	98.34 ± 2.15	95–105
	Hidden Valley	10	122.80 ± 16.48	107–163
Water (µg liter)	Virginia Foothills	17	51.24 ± 12.74	33–76
	Fairfax	17	<6.0	

[a] Standard error of mean. [b] No standard deviation given.

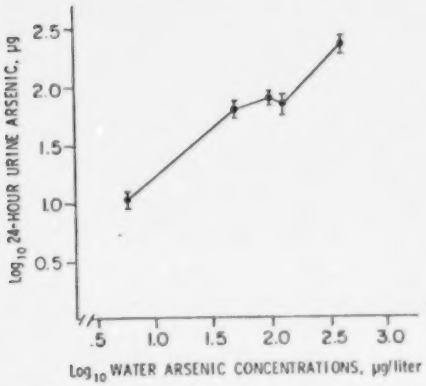

FIG. 2. Mean urinary arsenic concentration plotted as a function of mean arsenic concentration in tap water for compared communities. The bars represent standard error of mean.

follow this pattern, although a distinct rise in mean blood arsenic concentration in the Edison population was observed.

The Student's *t* statistic was used for determinations of statistical significance for the trends observed for body samples compared to water for each community (Table 3). Water arsenic concentrations for each community were found to significantly differ from each other. The statistically significant difference in water concentration obtained between Hidden Valley and Fallon can be ignored in practical terms when compared with the drinking water standard. Both communities were considered equal and at a concentration of 100 µg/liter. In Virginia Foothills, the population had received a water supply of 100 µg/liter consistently until approximately 4 months before the survey, due to poor operation of a treatment plant. Thus although the water concentrations there did show a statistically significant

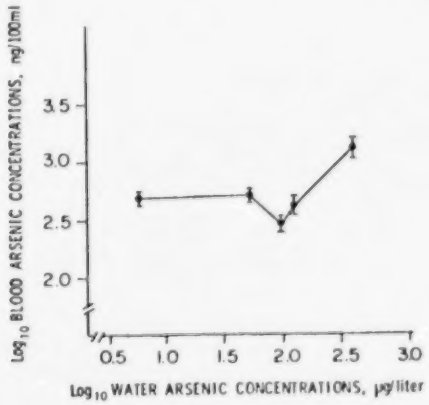

FIG. 3. Mean blood arsenic concentration plotted as a function of mean arsenic concentration in tap water for compared communities. The bars represent standard error of mean.

TABLE 3
STUDENT'S *t* TEST STATISTIC AND CORRESPONDING LEVEL OF SIGNIFICANCE FOR ARSENIC CONCENTRATIONS IN WATER AND BIOLOGICAL SPECIMENS OF COMPARED COMMUNITIES

Sample	Community	Virginia Foothills	Hidden Valley	Fallon	Edison
Water	Fairfax	−20.1 (<0.001)[a]	−54.9 (<0.001)	−321.8 (<0.001)	−86.9 (<0.001)
	Virginia Foothills	—	−18.5 (<0.001)	−18.9 (<0.001)	−58.3 (<0.001)
	Hidden Valley	—	—	7.6 (<0.001)	−45.5 (<0.001)
	Fallon	—	—	—	−55.6 (<0.001)
Blood	Fairfax	−0.19 (>0.05)	1.44 (>0.05)	4.76 (<0.001)	−4.09 (<0.001)
	Virginia Foothills	—	0.68 (>0.05)	2.02 (<0.05)	−3.44 (<0.001)
	Hidden Valley	—	—	2.81 (<0.01)	−4.36 (<0.001)
	Fallon	—	—	—	−5.04 (<0.001)
Hair	Fairfax	−3.45 (<0.01)	−3.98 (<0.001)	−5.40 (<0.001)	−7.25 (<0.001)
	Virginia Foothills	—	−0.16 (>0.05)	−0.76 (>0.05)	−4.24 (<0.001)
	Hidden Valley	—	—	−0.58 (>0.05)	−4.23 (<0.001)
	Fallon	—	—	—	−3.96 (<0.001)
Urine	Fairfax	−5.15 (<0.001)	−8.60 (<0.001)	−8.54 (<0.001)	−6.14 (<0.001)
	Virginia Foothills	—	−0.53 (>0.05)	−1.44 (>0.05)	−4.24 (<0.001)
	Hidden Valley	—	—	−0.87 (>0.05)	−3.65 (<0.001)
	Fallon	—	—	—	−4.88 (<0.001)

[a] Values in parentheses are the corresponding level of significance for the given *t* statistic.

difference by the *t* statistic, it was questionable as to whether the body sample concentrations from Virginia Foothills would be expected to be equal to those from Fallon and Hidden Valley communities.

The communities of Fairfax and Virginia Foothills had water arsenic concentrations at or below the standard and blood arsenic concentrations showed no statistical difference between them. However, when the same two communities were each compared with Hidden Valley, which had a significantly higher arsenic concentration by a factor of at least 2.5, again no significant difference in blood arsenic was found. A significant difference in blood arsenic was found for the Hidden Valley and Virginia Foothills populations when compared with the population of Fallon, but the level of significance was only $P < 0.01$ and $P < 0.05$, respectively, for the two community pairs. In comparison of each of the four

communities with Edison, which had from 3.2 to 65 times as much water arsenic, blood arsenic concentrations were significantly lower in each case.

In contrast to comparisons of blood levels, hair and urine arsenic concentrations for Virginia Foothills, Hidden Valley, and Fallon showed no statistically significant difference by the Student's *t* test. The Fairfax population, which had the lowest water arsenic concentration and served as the control community, showed a significant difference from the other four populations. The Edison population, which received the most arsenic via water, showed a statistically significant difference from all four for arsenic concentrations in hair and urine.

DISCUSSION AND CONCLUSIONS

Arsenic levels in blood, urine, and hair have been measured previously in nonexposed and exposed persons. However, rarely have several body samples been analyzed simultaneously and never in sufficient detail to determine which tissue would best reflect body burden.

Our results show that hair and urine mirror intake. The Virginia Foothills population received a water supply containing 100 μg/liter arsenic up until 4 months prior to our survey. At that time the arsenic concentration was lowered to approximately 50 μg/liter due to water treatment. The finding that the Virginia Foothills population had hair arsenic values that were not statistically significantly different from those of hair samples of the Fallon and Hidden Valley populations is plausible since the entire hair sample was taken for analysis. However, the absence of a statistically significant difference for urine concentrations among the same three populations raises questions. Mealey *et al.* (1959) found that after the intravenous injection of radioactive arsenic (trivalent form) into five human subjects only 2% of the initial excreted level remained in the urine at the end of 24 hr. However, his study represents the case of an acute exposure (single dose) where a significant body burden may not have developed. The question remains whether or not one would expect an elevated urine arsenic concentration 4 months later for a population which had been chronically exposed for an average 4-year time period. No studies have looked at such a relationship of long-term exposure to arsenic excretion. Such an attempt should be made in animal experiments to provide such answers.

Blood gave variable results for the lower levels of arsenic exposure. Once a higher level of intake occurred, blood arsenic also became elevated. Valentine and co-workers (1978) found a similar response of selenium concentrations in blood compared with hair and urine for a population exposed to varying levels of selenium via water from individual wells. Response of blood selenium was variable, while hair and urine reflected increased intake. They concluded that for selenium, blood does not reflect exposure unless chronic toxicity is reached. The same seems to hold true for arsenic concentrations in blood.

Heyman and co-workers (1956) found that hair arsenic concentrations in the range of 1 to 5 μg/g reflect chronic poisoning. The mean and range concentrations for the Edison population would suggest that chronic toxicity exists there. Such a finding for hair levels supports the conclusion that blood levels of arsenic mirror intake only when chronic toxicity is reached.

Goldsmith (1972) determined that at levels of arsenic in the drinking water

greater than 50 μg/liter an increase in the body, i.e., hair, resulted. Hair levels greater than 0.1 μg/g were found when such an elevation occurred. Our data agree. However, the levels in hair reported by Goldsmith and here for a water exposure up to 100 μg/liter are at the levels previously reported by others as normal.

In conclusion, blood does not seem to be useful in assessing the degree of exposure to arsenic. Hair and/or urine are more useful. In addition, it seems that chronic toxicity levels of arsenic are reached for a level of arsenic in drinking water somewhere between 100 and 400 μg/liter. However, such a conclusion needs to be substantiated (by obtaining health data on populations consuming such waters) before a statement can be made asserting the safety of 100 μg/liter of arsenic in drinking water.

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